I CLAIM:

1. A method for inducing differentiation of monocytes contained in an extracorporeal quantity of a subject's blood into functional dendritic antigen presenting cells, said method comprising the steps of:

(a) treating the monocytes by at least one of the following: (1) exposing the monocytes to physical perturbation, (2) irradiating the monocytes in the presence of a photoactivatable agent capable of forming photoadducts with cellular DNA components, and (3) treating the monocytes with a DNA binding agent; and

(b) incubating the treated monocytes for a period of time sufficient to maximize the number of functional dendritic cells.

2. The method of claim 1, wherein prior to step (a) the method further comprises the step of:

separating the monocytes from the extracorporeal quantity of the subject's blood by subjecting the quantity of blood to a leukapheresis process.

3. The method of claim 2, wherein the monocytes are incubated for a period of from about 6 to about 48 hours.

4. The method of claim 3, wherein the monocytes are incubated for a period of from about 12 to about 24 hours.

5. The method of claim 3, wherein the monocytes are irradiated in the presence of the photoactivatable agent.

6. The method of claim 6, wherein the photoactivatable agent is 8-MOP.

7. The method of claim 3, wherein the monocytes are exposed to the DNA binding agent.

8. The method of claim 3, wherein the treated monocytes are incubated together with at least one of GM-CSF and IL-4.

9. The method of claim 3, wherein the monocytes are incubated in a container which does not leach substantial amounts of plasticizer and which is sufficiently porous to permit exchange of gases.

10. The method of claim 3, wherein the treated monocytes are incubated together with at least one selected antigen to be processed and presented by the dendritic cells.

11. The method of claim 10, wherein the at least one antigen is expressed on the surface of a disease effector agent.

12. The method of claim 11, wherein the disease effector agent is selected from the group consisting of disease-causing cells and microbes.

Sub B'

13. A composition comprising functional dendritic antigen presenting cells derived from monocytes which have been incubated following their treatment by at least one of: (1) exposure to physical perturbation, (2) irradiation in the presence of a

photoactivatable agent capable of forming photoadducts with cellular components, and (3) treatment with a DNA binding agent.

14. The composition of claim 13, wherein the treated monocytes have been incubated for a period of time sufficient to maximize the number of functional dendritic cells present in the composition.

15. The composition of claim 14, wherein the treated monocytes have been incubated for a period of from about 6 to about 48 hours.

16. The composition of claim 15, wherein the monocytes have been incubated for a period of from about 12 to about 24 hours.

17. The composition of claim 14, wherein the monocytes have been irradiated in the presence of the photoactivatable agent.

18. The composition of claim 17, wherein the photoactivatable agent is 8-MOP.

19. The composition of claim 14, wherein the monocytes have been exposed to the DNA binding agent.

546 B2 20. The composition of claim 14, further comprising at least one of GM-CSF and IL-4.

5502450.1

21. The composition of claim 14 further comprising at least one selected antigen for presentation by the dendritic cells.

22. The composition of claim 21, wherein the at least one antigen is expressed on the surface of a disease effector agent.

Sub B3 23. The method of claim 22, wherein the disease effector agent is selected from the group consisting of disease-causing cells and microbes.

24. A packaged preparation comprising:

a composition including functional dendritic antigen presenting cells derived from monocytes which have been incubated following their treatment by at least one of exposure to physical perturbation, irradiation in the presence of a photoactivatable agent capable of forming photoadducts with cellular components, and treatment with a DNA binding agent; and

a container which does not leach substantial amounts of plasticizer and which is sufficiently porous to permit exchange of gases for storing the composition.

25. The packaged preparation of claim 24, wherein the treated monocytes have been incubated for a period of time sufficient to maximize the number of functional dendritic cells present in the composition.

26. The packaged preparation of claim 25, wherein the composition further includes at least one of GM-CSF and IL-4.

27. The packaged preparation of claim 25, wherein the composition further includes at least one selected antigen for presentation by the dendritic cells.

28. A method of enhancing the presentation of disease associated antigens, said method comprising the steps of:

(a) treating disease effector agents capable of expressing at least one disease associated antigen to one of: render the agents apoptotic and inactivate the agents;

(b) treating monocytes contained in an extracorporeal quantity of a subject's blood by at least one of the following: (1) exposing the monocytes to physical perturbation, (2) irradiating the monocytes in the presence of a photoactivatable agent capable of forming photoadducts with cellular components, and (3) treating the monocytes with a DNA binding agent; and

(c) incubating the treated disease effector agents and the treated monocytes together for a period of time sufficient to induce differentiation of the monocytes into functional dendritic antigen presenting cells and to optimize processing and presentation of the disease associated antigens by the dendritic cells.

29. The method of claim 28, wherein the treated disease effector agents and the treated monocytes are incubated together for a period of from about 6 to about 40 hours.

30. The method of claim 29, wherein the treated disease effector agents and the monocytes are incubated together for a period of from about 12 to about 24 hours.

31. The method of claim 28, wherein the disease effector agents are contained in the extracorporeal quantity of the subject's blood.

32. The method of claim 28, wherein the disease effector agents are derived from an exogenous source.

33. The method of claim 31, wherein prior to step (a) the method further comprises the step of:

separating the disease effector agents and the monocytes from the extracorporeal quantity of the subject's blood by subjecting the quantity of blood to a leukapheresis process.

34. The method of claim 28, wherein the disease effector agents are selected from the group consisting of disease-causing cells and microbes.

35. The method of claim 34 wherein the disease-causing cells selected from the group consisting of T-cells, B-cells and macrophages.

36. The method of claim 35, wherein the T-cells include lymphoma cells.

37. The method of claim 36, wherein the lymphoma cells include cutaneous T-cell lymphoma cells.

38. The method of claim 28, wherein steps (a) and (b) are performed simultaneously by irradiating the disease effector agents and the monocytes with a photoactivatable agent capable of forming photoadducts with DNA and cell proteins.

39. The method of claim 38, wherein the photoactivatable agent is 8-MOP.

40. The method of claim 28, wherein the disease associated antigen is selected from the group consisting of viral antigens, fungal antigens, bacterial antigens, transplant antigens and tumor specific antigens.

41. The method of claim 40, wherein the tumor specific antigen is a peptide derived from a T cell antigen-binding cell surface receptor.

42. The method of claim 28, wherein the disease effector agents and the monocytes are incubated together with at least one of GM-CSF, IL-4, TNF-alpha, and IL-12.

43. The method of claim 28, wherein the disease effector agents and the monocytes are incubated together in a container which does not leach substantial amounts of plasticizer.

44. The method of claim 28, further including the step of:

administering the incubated disease effector agents and the dendritic cells to the subject to elicit an immune response.

45. The method of claim 44, wherein the incubated disease effector agents and the dendritic cells are administered to the subject in at least one of the presence of and in combination with an immunomodulatory agent.

Sub B4

46. A composition of co-incubated populations comprising:

a first population including disease effector agents which express at least one disease associated antigen; and

a second population including functional dendritic antigen presenting cells derived from monocytes which have been treated by at least one of: (1) exposure to physical perturbation, (2) irradiation in the presence of a photoactivatable agent capable of forming photoadducts with cellular components, and (3) treatment with a DNA binding agent.

47. The composition of claim 46, wherein the first and second populations have been co-incubated for a period of from about 6 to about 40 hours.

48. The composition of claim 47, wherein the first and second populations have been co-incubated for a period of from about 12 to about 24 hours.

49. The composition of claim 46, wherein the disease effector agents are selected from the group consisting of disease-causing cells and microbes.

50. The composition of claim 49, wherein the disease-causing cells are selected from the group consisting of T-cell, B-cells and macrophages.

51. The composition of claim 50, wherein the T-cells include lymphoma cells.

52. The composition of claim 51, wherein the lymphoma cells include cutaneous T-cell lymphoma cells.

53. The composition of claim 46, wherein the disease effector agents and the monocytes have been treated with a photoactivatable agent.

54. The composition of claim 53, wherein the photoactivatable agent is 8-MOP.

55. The composition of claim 46, wherein the disease effector cells and the monocytes have been treated with a DNA binding agent.

56. The composition of claim 46, wherein the monocytes are separated from an extracorporeal quantity of a subject's blood.

57. The composition of claim 56, wherein the disease effector agents are one of contained in the extracorporeal quantity of the subject's blood and derived from an exogenous source.

58. The composition of claim 46, wherein the disease associated antigen is selected from the group consisting of viral antigens, fungal antigens, bacterial antigens, transplant antigens, and tumor specific antigens.

59. The composition of claim 46, further including at least one immunomodulatory agent.

Sub B5 ~~60. A packaged composition of co-incubated populations comprising:~~

a first population including disease effector agents which express at least one disease associated antigen;

a second population including functional dendritic antigen presenting cells derived from monocytes which have been treated by at least one of: (1) exposure to physical perturbation, (2) irradiation in the presence of a photoactivatable agent capable of forming photoadducts with cellular components, and (3) treatment with a DNA binding agent; and

a container which does not leach substantial amounts of plasticizer and which is sufficiently porous to permit exchange of gases for storing the composition.

61. A method of providing a vaccine against disease effector agents capable of expressing at leaset one disease associated antigen, said method comprising the steps of:

(a) treating the disease effector agents to one of: render the agents apoptotic and inactivate the agents;

(b) treating monocytes contained in an extracorporeal quantity of a subject's blood by at least one of the following: (1) exposing the monocytes to physical perturbation, (2) irradiating the monocytes in the presence of a photoactivatable agent capable of forming photoadducts with cellular components, and (3) treating the monocytes with a DNA binding agent;

(c) incubating the treated disease effector agents and the treated monocytes together for a period of time sufficient to induce differentiation of the monocytes into functional dendritic antigen presenting cells and to optimize processing and presentation of the disease associated antigens by the dendritic cells; and

(d) administering the incubated disease effector agents and the dendritic cells to the subject to vaccinate the subject against the disease effector agents.

62. The method of claim 61, wherein the disease effector agents are selected from the group consisting of disease-causing cells and microbes.

63. The method of claim 61, wherein the disease effector agents are one of: contained in the extracorporeal quantity of the subject's blood and derived from an exogenous source.

add B67

09924994 . 040202